Remarks

Claims 1, 8-16 and 18-42 are pending. By this amendment, applicants amend claims 1, 8-13, 16, 18-40; cancel claim 41 without prejudice and without disclaimer; and add new claims 43-74. Claim 42 has been withdrawn from consideration without prejudice and without disclaimer.

Support for the amendments made herein may be found throughout the specification as filed. No new matter has been added or introduced by these amendments to the specification or to the claims. Applicants respectfully request reconsideration of the subject application based on the following remarks.

I. Declaration Under 37 C.F.R. §1.67(a)

The Examiner states that the oath or declaration originally filed with the application is defective because it does not identify U.S. Provisional Application No. 60/032,329, which is identified in the application transmittal form filed with the subject application on December 3, 1997 as an application from which Applicants claim benefit under 35 U.S.C. §119(e).

In response, Applicants submit herewith a newly executed Declaration and Power of Attorney identifying the provisional application for which benefit under 35 U.S.C. §119(e) is desired, in compliance with 37 C.F.R. §1.67(a). The new Declaration and Power of Attorney identifies the provisional application by application number (60/032,329) and filing date (December 3, 1996). Applicants believe that the objection has been obviated by this submission and respectfully request that it be withdrawn.

II. Substitute Specification

The Examiner states that a substitute specification, including claims, is required because the interlineations and/or cancellations made in the specification, or amendments made to the claims, make the application difficult to consider.

Accordingly, Applicants submit herewith a substitute specification, including substitute claims, pursuant to the requirements of 37 C.F.R. §1.125(a). In compliance with 37 C.F.R. §1.125(b) and (c), both a clean copy of the substitute specification and a marked-up version showing changes made relative to the originally filed application are attached hereto. The substitute specification reflects all amendments previously entered under 37 C.F.R. §1.121, as well as additional amendments made herein to the specification and to the claims. Applicants note that the specification has been amended herein to contain a specific reference to the provisional application (60/032,329 which was filed on December 3, 1996) in the first sentence of the specification. The specification has also been amended to delete an erroneous reference to NIH grant support. The specification has also been amended herein to correct minor typographical errors. The substitute specification contains no new matter.

III. Claim Objections

Claim 16 is objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants have amended Claim 16 to depend upon Claim 8 instead of upon Claim 15, and to recite that the antagonist is "prepared from a previously lyophilized preparation". Applicants believe that the objection has been obviated by this amendment and respectfully request that it be withdrawn.

IV. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 27-30, 35, 36 and 39

Claims 27-30, 35, 36 and 39 are rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the specification was filed, had possession of the claimed invention. Specifically, the Examiner states that the specification does not provide a basis for claiming "a polypeptide that interferes with the

biological activity of GIP wherein said polypeptide comprises an amino acid sequence corresponding to amino acids 16-30, 21-30, or 7-9 of GIP".

Applicants have amended claims 27-30, 35, 36 and 39. Applicants believe the rejections have been obviated by these amendments and respectfully request reconsideration.

Claims 1, 8-12, 15, 16, 18, and 19

Claims 1, 8-12, 15, 16, 18, and 19 are rejected under 35 U.S.C. §112, first paragraph. The Examiner states that the specification, while being enabling for an antagonist of GIP consisting essentially of amino acids 7-30 or 10-30 of rat GIP, does not reasonably provide enablement for an antagonist of GIP without regard to the structure thereof, effective alternative sequences thereto, or for antagonistic polypeptides comprising other than amino acids 7-30 or 10-30. The Examiner also states that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims.

Applicants have amended claims 1, 8-12, 16, 18, and 19. Applicants believe the rejections have been obviated by these amendments and respectfully request reconsideration.

Claims 11-14, 20, and 21

Claims 11-14, 20, and 21 are rejected under 35 U.S.C. 112, first paragraph. The Examiner states that the specification, while being enabling for reducing glucose absorption, does not reasonably provide enablement for preventing, inhibiting, or reducing obesity.

Applicants have amended claims 11-13, 20, and 21. Applicants believe the rejections have been obviated by the amendments to claim 11 and respectfully request reconsideration.

V. Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected the following claims under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which application regards as the invention.

Claim 9 is rejected over the recitation of "posts 7-30 of the sequence". The Examiner states that the metes and bounds of the claim are not clearly set forth. Applicants have amended Claim 9, without prejudice, to delete the phrase "posts 7-30 of the sequence". Applicants believe the rejection has been obviated by this amendment to Claim 9 and respectfully request reconsideration.

Claims 9, 12, 18, 20, 23, 25, 27, 29, 31, 33, 35, and 37 are rejected as indefinite over the recitation of "effective number of amino acids". The Examiner states that it is unclear what effect is achieved by the effective number. Applicants have amended these claims, without prejudice, to delete the recitation of "effective number of amino acids". Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

Claims 9, 10, 12, 13, 18-21, 23-28, 40 and 41 are rejected as indefinite over the recitation of "effective alternative sequences" because it is unclear what effect is achieved by the effective alternative sequences. Applicants have amended these claims, without prejudice, to delete the recitation of "effective alternative sequences". Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

Claims 11-14, 20 and 21 are rejected as indefinite. The Examiner states that it is unclear if inhibiting, blocking, or reducing glucose adsorption is synonymous with preventing, inhibiting, or reducing obesity or whether some other effect is intended. Applicants have amended claims, without prejudice, 11-14, 20 and 21. Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

Claims 22 and 39 are rejected as indefinite over the recitation of "effective amount" because it is unclear what effect is intended by an "effective amount". Applicants have amended claims 22 and 39, without prejudice, to delete the phrase "effective amount". Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

Claims 22-41 are rejected as indefinite over the recitation of the acronym "GIP" because the meaning of "GIP" is ambiguous. Applicants have amended Claims 22 and 39, without prejudice, to spell out the acronym as "glucose-dependent insulinotropic polypeptide". Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

Claim 36 is rejected as indefinite. The Examiner states that it is unclear if the polypeptide comprises 10 contiguous or non-contiguous amino acids of the sequence. Applicants have amended Claim 36, without prejudice. Applicants believe the rejection has been obviated by this amendment and respectfully request reconsideration.

Claims 1, 9, 10, 12, 13, 18-21 and 23-41 are rejected as indefinite because they recite the term "corresponding to". The Examiner states that because the specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "corresponding to", an artisan cannot determine what additional material and/or functional limitations are placed upon a claim by the presence of this term. Applicants have amended Claims 1, 9, 10, 12, 13, 18-21 and 23-41, without prejudice, to delete the phrase "corresponding to". Applicants believe the rejection has been obviated by these amendments and respectfully request reconsideration.

With respect to the Examiner's §112 rejections, it is respectfully submitted that such rejections are not applicable to the currently pending claims or the specification. More specifically, it is respectfully submitted that the specification as originally filed does provide a written description and is enabling for the claims now pending. By way of example and support, the effects of at least four GIP polypeptide receptor inhibitors have been demonstrated, in the originally filed application. Moreover, the data teach which segments (and therefore structure)

one skilled in the art would use to make a genus of effective GIP antagonists. In fact, the specification in original paragraph 0035 and in Examples 1 and 3-5 specifically teach one skilled in the art how to make a genus of effective GIP antagonists. To further support that the specification meets the written description and enablement requirements under 35 U.S.C. 112, applicants are willing to submit §1.132 declarations from those who have worked in the field and are recognized as skilled practitioners in closely related areas of protein chemistry and structure as well as in molecular pharmacology of receptor binding and inhibitor design to assist the examiner, if deemed necessary by the Examiner, in determining the effect of the specification in teaching others how to make and use the invention without undue experimentation.

VI. Rejection Under 35 U.S.C. §102(a) - Gelling

Claims 1, 8, 9, 10, 18, 19 and 22-41 are rejected under 35 U.S.C. §102(a) as being anticipated by Gelling. The Examiner states that Gelling teaches porcine $GIP_{10\text{-}30,\ 6\text{-}30,\ 7\text{-}30}$ antagonistic peptides, and that porcine $GIP_{6\text{-}30}$ consist essentially of a 24 amino acid polypeptide corresponding to positions 7-30 of SEQ ID NOS: 2 and 8, or effective alternative sequences thereto.

Applicants note that the present application claims priority to U.S. Provisional Application Serial No. 60/032,329, which was filed on December 3, 1996. As indicated above, Applicants have amended the specification herein to contain a reference to the prior provisional application. Applicants would like to respectfully direct the Examiner's attention to M.P.E.P. §706.02, which states, "[I]f the application is entitled to priority under 35 U.S.C. §119(e) from a provisional application, the effective filing date is the filing date of the provisional application." Because the effective priority date of the above-identified application for U.S patent is December 3, 1996, the subject application predates the publication date of Gelling (i.e., April 30, 1997). It is therefore respectfully submitted that Gelling does not and can not constitute prior art to the present application as defined by 35 U.S.C. §102. Accordingly, Applicants believe that the Gelling reference should be removed as prior art and respectfully request that this rejection be withdrawn.

VII. Rejection Under 35 U.S.C. §102(b) – Ebert

Claims 1, 8-14, and 18-41 are rejected under 35 U.S.C. §102(b) as being anticipated by Ebert. The Examiner states that Ebert teaches a specific GIP antiserum that comprises an antibody or antibodies that is or are an antagonist of GIP, consists essentially of or comprises a 24 amino acid polypeptide corresponding to any position of the sequence of GIP, or comprise at least an effective number of amino acids corresponding to those amino acids in any position of GIP, or effective alternative sequences thereto, because the metes and bounds of "corresponding to" are not clearly set forth, and because there are no structural or functional limitations to "effective alternative sequences thereto". The Examiner further states that Ebert teaches a pharmaceutical composition comprising the anti-GIP antagonistic antibody or antibodies.

Applicants respectfully disagree. The present application teaches that postprandial (1) glucose uptake from the gut, (2) insulin release from the pancreas, (3) insulin blood levels *and* (4) glucose blood levels all decrease following administration of GIP antagonist in accordance with the present invention (see, for example, Figs. 6-9). Consistent with Figs. 6-9, the specification teaches that, for example, a significant decrease in blood glucose levels is achieved even though insulin blood levels were diminished (see, substitute specification, paragraph [0030]). This is quite surprising and very unexpected, especially in view of traditional thinking, i.e., one would expect to see an increase in glucose blood levels when there is a decrease in insulin release, not a decrease in glucose blood levels when there is a decrease in insulin release, as demonstrated by the present invention.

In contrast to the present invention as now claimed, it is respectfully submitted that Ebert in fact teaches away from the present invention, as now claimed. More specifically, Ebert teaches to increase the serum glucose and decrease the plasma insulin, which is the exact opposite effect of Applicants' present invention. In this regard, the Examiner is specifically directed to Fig. 2, Fig. 3, Table 2 and Fig. 4 in Ebert. In Fig. 2 of Ebert (Ebert, p. 1604), Ebert teaches that serum glucose levels increase and insulin levels decrease when the alleged Ebert "GIP antiserum" is administered. In Fig. 3 (Ebert, page 1604) and in Table 2 (Ebert, page 1604), Ebert again teaches that upon administration of the alleged Ebert "GIP antiserum," insulin levels

decrease and serum glucose levels increase. Consistent with Figs. 2 and 3 and Table 2, Ebert teaches in Fig. 4 that plasma glucose levels increase and insulin levels decrease upon administration of the alleged "GIP antiserum".

In summary, Ebert does not teach to decrease serum glucose levels when the alleged Ebert "GIP antiserum" is administered. Rather, Ebert teaches away from and underscores the novelty and patentability of Applicants' invention, as now claimed. Accordingly, the Ebert reference fails to teach or suggest the limitations of the present claims under 35 U.S.C. §102 or §103, respectively.

Furthermore, the Examiner states that eliminating terms such as "corresponding to" and/or "effective alternates thereto" would overcome the prior art of Ebert. Applicants have amended Claims 1, 8-14, and 18-41, without prejudice, to remove these phrases. Applicants believe that these amendments and the arguments made above obviate the rejection and respectfully request reconsideration.

VIII. Rejection Under 35 U.S.C. 103(a)

Gelling or Ebert in view of Avis and/or Turco

Claims 8, 15, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gelling or Ebert, as applied to Claim 8, and further in view of Avis and/or Turco.

In response, Applicants note that the Gelling reference is removed an does not qualify as prior art pursuant to the explanation above regarding priority data. Therefore, it is improper to cite Gelling in a rejection under 35 U.S.C. 103(a). Furthermore, Ebert fails to teach or suggest the limitations of the present claims, as explained above. Because neither Avis nor Turco alone or in any appropriate combination cure the deficiencies of Ebert, and the appropriate combination of Ebert in view of Avis and/or Turco do not suggest the inventions as now claimed in amended claims 8, 15 and 16, Applicants believe that the rejection is obviated and rendered moot. Reconsideration is therefore respectfully requested.

Gelling in view of Turco

Claims 11-14, 20 and 21 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gelling as applied to claims 1, 8, 9, 10, 18, 19 and 22-41, and further in view of Turco, as applied to claims 8, 15, and 16.

Applicants again note that Gelling does not constitute prior art to the present invention. Therefore, it is respectfully submitted that it is improper to cite Gelling alone or in combination with Turco, in a rejection under 35 U.S.C. §§103(a). Because Turco does not teach or suggest the inventions as claimed in amended claims 11-14, 20 or 21, Applicants believe that the rejection is obviated and reconsideration is respectfully requested.

IX. Conclusion

For each and all of the foregoing reasons and in view of the foregoing Amendment, it is respectfully submitted that currently pending Claims 1, 8-16 and 18-41 as hereinabove amended and new Claims 42-88 are in condition for allowance. Therefore, favorable reconsideration and allowance of this application is earnestly solicited.

A check for the fees required for the Request for Continued Examination ($385.00) and for the five-month extension time ($1,005.00) are enclosed. The Commissioner is hereby authorized to charge the fee for new clams ($1,487.00) to Deposit Account No. 04-1105. Applicants believe that no additional fees are required in connection with this submission. If a fee is required, a fee paid is inadequate, or credit is owed for any excess fee paid, the Commissioner is hereby authorized to charge/credit Deposit Account No. 04-1105.

If the undersigned can be of any assistance in advancing the prosecution of this case, the Examiner is invited to telephone the undersigned at the numbers given below.

Respectfully submitted,

Date: 29-3-2004 By: _____

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